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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/298,508	04/22/99	ECHELARD Y	10275/122001

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EXAMINER	
WOITACH,J	
ART UNIT	**PAPER NUMBER**
1632	10

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Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

File

Office Action Summary	Application No. 09/298,508	Applicant(s) Echelard, Y. et al.
	Examiner Joseph Woitach	Group Art Unit 1632

☐ Responsive to communication(s) filed on _____.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire 3 month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) 1-91 is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) 1-91 is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☒ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☒ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). 7,8

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- *SEE OFFICE ACTION ON THE FOLLOWING PAGES* ---

DETAILED ACTION

This application is an original application filed April 22, 1999, which claims benefit to application 60/106,728 filed November 2, 1998. Claims 1-91 are pending and under current examination.

Oath/Declaration

The oath or declaration is defective. A new oath or declaration in compliance with 37 CFR 1.67(a) identifying this application by application number and filing date is required. See MPEP §§ 602.01 and 602.02.

The oath or declaration is defective because:

The full name of Esmail Behbodi does not match the signature Esmail Behboodi.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 6, 9, 16-18, 19-23, 36, 39, 46-48, 49-53, 66, 69, 76, 77-83 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Specifically:

Claims 6, 18, 36, 48, 66, 78 are unclear in the recitation of "disrupts the expression" because it is not clear if the transgene alters the expression levels of transcription or simply disrupts the contiguous sequence of the endogenous gene.

Claims 6, 18, 36, 48, 66, 78 are unclear in the recitation of "or other event" because it is not clear what is encompassed within the metes and bounds of the claim. While transgenic knockout and knockin terminology is defined in the specification and known in the art, other events related to a transgene which would disrupt the expression of an endogenous gene are not clearly defined.

Claims 9, 21, 39, 51, 69, 81 are unclear in the recitation of "milk-specific promoter" because it is unclear if the promoter is responsive to milk or that the promoter is active in the mammary gland during lactation as suggested by the group of promoters listed in dependent claims 10, 22, 39, 52, 70 and 82.

Claims 16, 46 and 76 are unclear and confusing because it recites that the heterologous nucleic acid of the dependent claim should be heterologous. For example, claim 16 does not further limit claim 14. Claims 46 and 76 are also rejected for the same reason.

Claims 17, 47 and 77 are unclear in the recitation of "human sequence" because the metes and bounds of what constitutes a human sequence are not clearly defined. The recited nucleic

acid does not have any size or functional limitations, so a sequence of 5 base pairs from a human gene would most likely find 100% homology with sequences form other species and it would be unclear what would differentiate these sequences.

Claims 19-23, 49-53, 79-83 are vague and unclear in the recitation of "the nucleic acid is under the control of a promoter" because a 'nucleic acid' does not necessarily maintain a function that can or would be regulated by a promoter. For example, short nucleic acid sequences of five base pairs would have no function in relation to the promoter.

Double Patenting

Applicant is advised that should claims 14, 44, 74 be found allowable, claims 16, 46, 76 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 28, 58, 88 are objected to under 37 CFR 1.75 as being a substantial duplicate of claims 27, 57, 87. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

Claims 1 and 31 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by ATCC number CCL-73.

Claims 1 and 31 encompass a purified embryonic or fetal caprine cell. ATCC number CCL-73 is a *Capra hircus* (goat) primary cell line derived from the esophagus of a male goat embryo at 2/3 term. The cell line has been used and referenced in at least two cited references (1967 and 1994, bottom of specification sheet). Thus the claims 1 and 31 are anticipated.

Claims 1, 31 and 61 are rejected under 35 U.S.C. 102(b) as being clearly anticipated by Amoah *et al.*

Claims 1 and 31 encompass a purified embryonic or fetal caprine cell. Claim 61 encompasses a method of preparing said cells. Amoah *et al.* teach the isolation of goat embryos at the morulae and blastocycts stages (page 580; first and second columns). Use of these methods

one can obtain a purified preparation of goat embryonic cells. Thus the claims 1, 31 and 61 are anticipated.

Claims 1-5, 7, 12-17, 19, 24-28, 31-35, 37, 42-47, 49, 54-58, 61-65, 67, 72-77, 79, 84-88 rejected under 35 U.S.C. 102(b) as being clearly anticipated by Archer *et al.*

The recited claims encompass a purified or purified preparation of embryonic or fetal caprine somatic cell wherein the cell comprises a transgene wherein the transgene comprises a heterologous sequence encoding a polypeptide selected from the group consisting of a hormone, an immunoglobulin, a plasma protein and an enzyme under the control of a promoter. Further, methods for preparing said cell with described embodiments are also recited. Archer *et al.* teach two sources of purified goat cells; Ch1Es cells and goat mammary epithelial (GME) cells. Ch1Es cells can be obtained from ATCC (ATCC listing attached) and represent fibroblast cells derived for a goat at 2/3 term. GME cells are primary somatic cells derived from adult early-lactation goats (page 6840; material and methods). Archer *et al.* also teach a method to derive GME cells. Archer *et al.* use two retroviral vectors containing the heterologous nucleic acid sequences encoding a transgene for hGH and β-galactosidase (page 6841; figure 1). These vectors are used to transduce said goat cells to create goat cells which contain a transgene and encode a polypeptide (pages 6842-3; Tables 2 , 3 and 4 and figure 3). Thus Archer *et al.* anticipate the claims.

Claims 61-91 are rejected under 35 U.S.C. 102(e) as being anticipated by Strelchenko *et al.*

Claim 61 encompasses a method of preparing an embryonic or fetal goat cell line comprising obtaining a somatic cell and culturing the cell in a suitable medium. Claims 62-91 recite further limitations wherein the cell is genetically engineered with a heterologous gene under the control of promoter. Strelchenko *et al.* teach a method of establishing a cultured cell (column 44; Example 2). As stated in the first paragraph of the method, the starting cell can be obtained from any type of cell including embryonic and fetal cells (column 44; lines 16-17) and from any animal (column 45; lines 13-15). Examples specific promoters, in particular milk protein promoters (column 12; lines 30-37), specific transgenes encoding specific polypeptides such as hormones, enzymes, plasma proteins and immunoglobulins are recited throughout the specification (for example column 36; lines 7-63). Finally, transgenic cells can be prepared from transgenic animals (columns 50-52; Example 8). Thus all the embodiments of claims 61-91 are anticipated by Strelchenko *et al.*

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person

having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 7-17, 19-35, 37-47, 49-60 are rejected under 35 U.S.C. 103(a) as being unpatentable over Archer *et al.* as applied to claims 1-5, 7, 12-17, 19, 24-28, 31-35, 37, 42-47, 49, 54-58 above, and further in view of Amoah *et al.*

Claims 1-5, 7, 12-17, 19, 24-28, 31-35, 37, 42-47, 49, 54-58 are summarized above. Claims 8-11, 38-41 50-53 encompass tissue specific promoters, in particular caprine milk-specific promoters. Claims 12-13, 24-25, 42-43, 54-55 encompass transgenes which encode a polypeptide selected from the group consisting of a hormone, an immunoglobulin, a plasma protein and an enzyme, and in particular the specific polypeptides listed in claim 13. Archer *et al.* teach isolated embryonic caprine somatic cells which have been transduced with a heterologous nucleic acid encoding a transgene wherein expression of the transgene is under the control of a promoter. Archer *et al.* teach the transgene hGH, a hormone, and β-galactosidase, an enzyme, and the LTR promoter, however they do not teach milk-specific promoters or all the specific transgenes recited in the claims. Amoah *et al.* teach promoters to specifically target expression of a transgene to the mammary gland (page 582; section on Gene Transfer). Further, in the same

section, Amoah *et al.* teach several of the specific transgenes recited in claim 13 which have already been used to produce transgenic goats and teach that other transgenes can also be expressed in the mammary gland. Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the methods of Archer *et al.* to isolate and create caprine cells with the promoters and transgenes described by Amoah *et al.* One having ordinary skill in the art would have been motivated to use the different transgene constructs described in Amoah *et al.* in addition or as an alternative to those described by Archer *et al.* to obtain cell specific expression of transgenes to improve the quality of animal products through genetic improvements or for the production of pharmaceuticals (Amoah page 578; first paragraph). There would have been a reasonable expectation of success given the results of Archer *et al.* in isolated embryonic or GME caprine cells, to obtain an isolated caprine cell with expression of transgenes under the control of milk-specific promoters as taught by Amoah *et al.*

Thus, the claimed invention as a whole was clearly *prima facie* obvious.

Claims 1-91 are rejected under 35 U.S.C. 103(a) as being unpatentable over Archer *et al.* in view of Amoah *et al.* as applied to claims 1-5, 7-17, 19-35, 37-47, 49-60 above, and further in view of Strelchenko *et al.*

Claims 61-91 are summarized above in the 35 U.S.C. 102 rejection. Claims 1-5, 7-17, 19-35, 37-47, 49-60 are summarized above in the 35 U.S.C. 103 rejection. The remaining claims 6, 18, 36 and 48 encompass a caprine cell which comprises a transgene wherein the transgene is a

knockout, knockin or other event which disrupts the expression of a caprine gene. Archer *et al.* teach isolated embryonic caprine somatic cells which have been transduced with a heterologous nucleic acid encoding a transgene wherein expression of the transgene is under the control of a promoter. Archer *et al.* teach a transgene which is randomly inserted, however they do not teach a transgene which has been targeted to insert into a specific nuclear DNA sequence. Strenlchenko *et al.* teach several recombinant DNA techniques known to a person of ordinary skill in the art which includes knockout and introducing base pair mutations into the target nuclear DNA (column 12; lines 38-67). Further, Strenlchenko *et al.* also teach promoters to specifically target expression of a transgene to the mammary gland (column 12; lines 26-37 and column 15; lines 20-31), and that one can express many types of genes of interest including hormones, enzymes and other pharmaceuticals and recite several of the specific transgenes (column 36; lines 6-67). Therefore, it would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to use the cells and methods of Archer *et al.* to isolate and create caprine cells with the promoters and transgenes described by Amoah *et al.* and Strenlchenko *et al.*, and to target transgene constructs to specific nuclear DNA sequences as taught by Strenlchenko *et al.* One having ordinary skill in the art would have been motivated to generate caprine cells containing knockout constructs described in Strenlchenko *et al.* to be used in the creation of transgenic goats through nuclear transfer (Strenlchenko- entire document). There would have been a reasonable expectation of success given the results of Strenlchenko *et al.* and

one of ordinary skill in the art to create caprine cells in which the nuclear DNA has been modified by insertion of a transgene.

Conclusion

No claim allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph Woitach, whose telephone number is (703) 305-3732. The examiner can normally be reached on Monday through Friday from 8:00 to 4:30 (Eastern time).

If attempts to reach the examine by telephone are unsuccessful, the examiner's supervisor, Karen M. Hauda, can be reached on (703) 305-6608. The fax number for group 1600 is 1 (800)308-4242.

An inquiry of a general nature or relating to the status of the application should be directed to the group receptionist whose telephone number is (703) 308-0196.

Joseph T. Woitach

Patent Examiner
AU 1632